



NOTES

ADULT PRIMARY BRAIN TUMORS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Diverse central nervous system cell neoplasms
 - Benign/malignant

RISK FACTORS

- Genetic predisposition
- Ionizing radiation exposure
- Dietary N-nitroso compounds (NOCs)

COMPLICATIONS

- **Mass effect:** hydrocephalus, ↑ intracranial pressure, herniation
- Neurocognition, motor dysfunction, death

SIGNS & SYMPTOMS

- Vary depending on tumor type
- May be asymptomatic; headache; visual, hearing deficits; nausea; vomiting; altered level of consciousness (LOC)

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Visualizes tumor mass

LAB RESULTS

- **Biopsy:** histopathologic, molecular examination

OTHER DIAGNOSTICS

- **Tumor grades:** World Health Organization (WHO) grading system

TREATMENT

- Dependent on tumor stage, grade

MEDICATIONS

- Steroids
- Monoclonal antibodies
 - Avastin
- Chemotherapy

SURGERY

- Resection

OTHER INTERVENTIONS

- Radiation

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GLIOBLASTOMA MULTIFORME (GBM)

osms.it/glioblastoma-multiforme

PATHOLOGY & CAUSES

- **Highly malignant**, aggressive glial cell tumor
- Location: usually hemispheric white matter
 - Mass with grayish periphery, necrosed yellow center, multiple bleeding zones
- World Health Organization (WHO) grade IV tumor

TYPES

Histology

- Giant-cell glioblastoma
 - Multinuclear, giant cells
- Gliosarcoma
 - Combined astrocytic, sarcoma-like components; squamous/gland-like structures → possible differentiation into other tissue
- Epithelioid glioblastoma
 - Eosinophilic cytoplasm in large epithelioid cells

Development-based

- Correlated with Isocitrate dehydrogenase (IDH) gene mutation
- Primary
 - Spontaneous development, individuals aged > 50
 - AKA IDH wild-type: no IDH gene mutation
- Secondary
 - Individuals aged < 50
 - Low-grade astrocytoma (WHO grade II)
 - Anaplastic astrocytoma (WHO grade III)

Subtypes: molecular characteristics

- Classic
 - Molecular changes resemble primary type

- Proneural
 - Secondary type gene mutations
- Neural
 - ↑ expression of NEFL, GABRA1, SYT1, SLC12A5 tumor markers
- Mesenchymal
 - ↓ NF1 gene, ↑ TNF and NF-κB pathway genes expression

CAUSES

- Genetic alterations

Primary GBM

- Epidermal growth factor receptor (EGFR) gene mutation → overexpression, constant receptor activation → uncontrolled cell proliferation
- Heterozygosity loss commonly affects long arm of chromosome 10
- Phosphatase, tensin homologue (PTEN) gene mutation → tyrosine phosphatase activity loss → overactivated signaling pathways → ↑ proliferation

Secondary GBM

- IDH1/IDH2 gene mutation → 2-hydroxyglutarate (2-HG) overproduction → impaired DNA methylation due to 2-HG
- TP53 mutation → tumor suppression function lost
- Heterozygosity loss on long arm of chromosomes 13, 19, 22
- Platelet-derived growth factor (PDGF) gene mutation with overexpression → ↑ PDGF receptor binding → ↑ proliferation

RISK FACTORS

- White, biologically-male individuals of Jewish descent, aged 45–70
- Genetically-inherited diseases
 - Li–Fraumeni syndrome, tuberous sclerosis, neurofibromatosis

- Radiation exposure
- Tobacco use
- Pesticide exposure
- Viruses
 - Simian virus 40, Human herpesvirus 6, Cytomegalovirus

COMPLICATIONS

- Extension to ventricular wall
- Meningeal gliomatosis
 - Malignant cell spread to spinal cord via cerebrospinal fluid (CSF)
- Recurrence
- Multifocality
- Mass effect
 - Obstructive hydrocephalus, ↑ intracranial pressure, herniation
- Seizures
 - Supratentorial glioblastoma

SIGNS & SYMPTOMS

- Severe morning headache, attenuates throughout day → focal symptomatology
 - Motor (gradual), sensory, vision loss; aphasia
- Mental changes
 - Altered mood, personality; impaired comprehension, concentration, memory

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Hypodense central area, irregular ring-like edge enhancements

MRI

- T1: hypointense center
- T2: hyperintense center, peripheral low-attenuated vasogenic edema

Magnetic resonance spectroscopy (MRS)

- ↑ choline, lactate, lipid peaks
- ↓ N-acetylaspartate, myo-inositol peaks

Positron emission tomography (PET)

- ↑ glucose metabolism

OTHER DIAGNOSTICS

Histology

- Inadequate astrocyte differentiation with atypical nuclei, uncontrolled cell proliferation with shape/size cell variation
- Immunostaining
 - Commonly positive glial fibrillary acidic protein (GFAP)

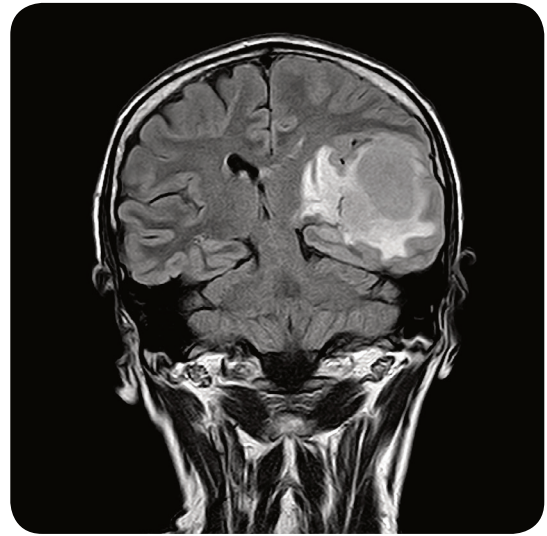


Figure 61.1 An MRI scan of the head in the coronal plane demonstrating glioblastoma of the left temporal lobe.

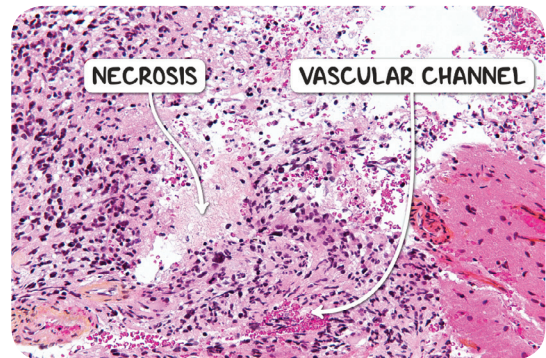


Figure 61.2 The histological appearance of a glioblastoma multiforme. The tumor is composed of malignant glial cells with marked nuclear pleomorphism. The tumor demonstrates necrosis and is forming microvascular channels.

TREATMENT

MEDICATIONS

- Avastin (common)

SURGERY

- Total/subtotal tumor resection

OTHER INTERVENTIONS

- Adjuvant chemotherapy, radiation therapy

HEMANGIOBLASTOMA

osms.it/hemangioblastoma

PATHOLOGY & CAUSES

- Benign tumor; **vascular cell proliferation**, new blood vessel formation
- **Cherry red** cystic/solid mass structure in cerebellum, spinal cord, brainstem
- WHO grade I tumor

CAUSES

Sporadic

- Usually solitary, cerebellum most commonly affected

Von Hippel–Lindau (VHL) disease

- Gene impairment with HL protein dysfunction → hypoxia inducing factor (HIF) build up → ↑ production of angiogenic factors, vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor (TGF) → stimulation of angiogenesis
- Small, multiple lesions
- Common spinal cord affection, retinal hemangiomas also occurs

RISK FACTORS

- Biologically-male individuals, aged 20–50

COMPLICATIONS

- Acute hemorrhage
 - **Intracerebral**: brainstem compression/ tonsillar herniation, obstructive hydrocephalus
 - **Spinal**: acute quadriplegia
- Tumor mass effect → ↑ intracranial pressure
- **Local structure compression**: neurologic deficits (e.g. oculomotor nerve dysfunction, motor weakness, sensory deficits)
- Paraneoplastic erythrocytosis → polycythemia

SIGNS & SYMPTOMS

- Tumor location-dependent
 - **Brainstem**: visual, sensory impairment; motor weakness
 - **Cerebellum**: ataxia
 - **Spinal cord**: pain, sensory impairment
- In von Hippel–Lindau disease (VHL)
 - Effect on retina → vision loss

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- T1 hypointense/T2 hyperintense mass with defined edges

CT scan

- Hypodense mass

Ultrasound

- Hyperechoic zones amid surrounding tissue

Angiography

- Preoperative tumor visualization

OTHER DIAGNOSTICS

Histology

- Two components
 - **Endothelial:** small endothelial cells with sparse cytoplasm
 - **Stromal:** cells with eosinophilic cytoplasm, numerous vacuoles

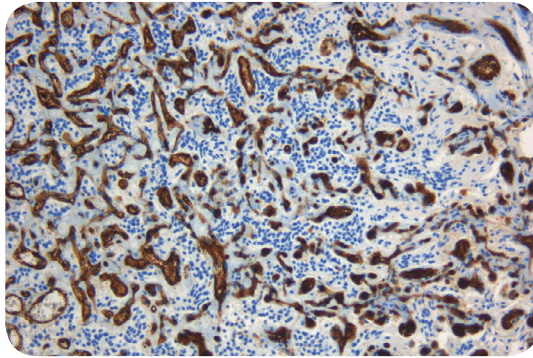


Figure 61.3 Immunohistochemical staining of a hemangioblastoma with CD31 highlights the endothelial component of the tumor (dark brown).

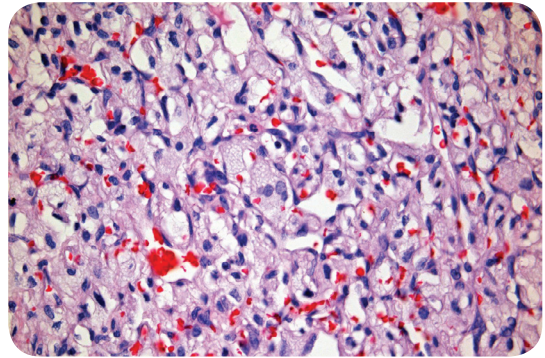


Figure 61.4 The histological appearance of a hemangioblastoma. The tumor is composed of numerous, closely-packed, thin-walled capillaries with underlying neoplastic stromal cells.

TREATMENT

MEDICATIONS

- Antiangiogenic treatment
 - ↓ EDGF production

SURGERY

- Excision
- Stereotactic radiosurgery

MENINGIOMA

osms.it/meningioma

PATHOLOGY & CAUSES

- Tumor arising from dome-shaped meningeal arachnoid cells with base on meninges
- Intracranial (usual), spinal (occasional)
- WHO grade I, II, III (morphology-dependent)

CAUSES

Sporadic

- TNF-receptor associated factor 7 (TRAF7) mutation

Genetic predisposition

- Long arm of chromosome 22 loss → NF2 tumor suppressor gene impairment
- SMARCB1 tumor suppressor gene mutation
- MEN1 tumor suppressor gene mutation

RISK FACTORS

Genetically-inherited diseases

- Neurofibromatosis type 2
 - Intracranial localization (usual), spinal meninges (occasional)
 - Associated with multiple meningiomas
- Schwannomatosis
- Multiple endocrine neoplasia type I (MEN I)

Ionizing radiation

- Radiation exposure, dental radiographs, diagnostic CT scan (children)

Other risk factors

- Obesity
- Black, biologically-female individuals of African descent more prone, ↑ incidence in later age

COMPLICATIONS

- Recurrent meningiomas
- Mass effect
 - Obstructive hydrocephalus, ↑ intracranial pressure, herniation
- Bone abnormalities
 - Reactive sclerosis, bone invasion/erosion possible (meningioma located on skull base)
- Seizures

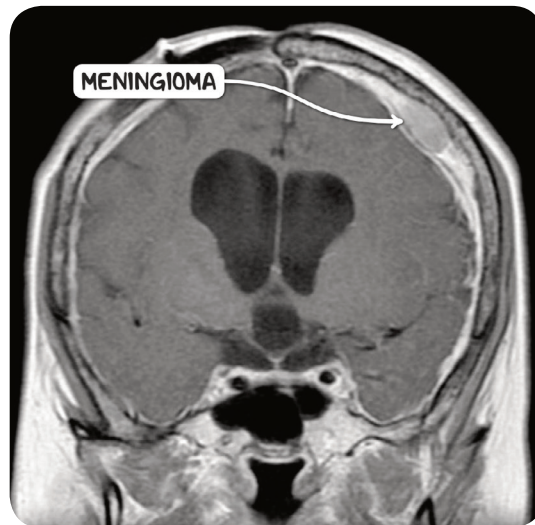


Figure 61.5 An MRI scan of the head in the coronal plane demonstrating a meningioma.

SIGNS & SYMPTOMS

- May be asymptomatic; very slow growth
- Symptoms tumor location-dependent

Visual impairment

- Sella turcica vicinity
 - One-sided papilledema, optic atrophy of other eye (Foster-Kennedy syndrome)
- Cavernous sinus meningiomas
 - Compression of cranial nerves supplying extraocular muscles → muscles

- weakness, double vision
- Optic nerve meningiomas
 - Gradual, monocular, vision loss

Impaired hearing and smell

- Cerebellopontine angle meningiomas
 - Sensorineural deafness
- Olfactory groove meningiomas: anosmia

Behavioral changes

- Apathy, impaired attention, impulsivity
- Usually subfrontal meningiomas

Muscle weakness

- Parasagittal meningiomas
 - Contralateral leg weakness
- Foramen magnum meningiomas
 - Lesion-side arm weakness → ipsilateral leg progression → contralateral leg affection → contralateral arm weakness
- Spinal cord meningiomas
 - One-sided plegia of extremities, sensory loss on other side (Brown–Séquard syndrome)



Figure 61.6 The histological appearance of a meningioma showing a typical whorled architecture.

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- T1 hypointense/T2 hyperintense dural-based mass, dural thickening with tail-like structure (“tail sign”)

CT scan

- Isodense mass, brain tissue compression

PET

- ↑ uptake of 18F-Fluorodeoxyglucose

OTHER DIAGNOSTICS

Histology

- WHO Grade I
 - Benign, not classified
- WHO grade II
 - Atypical, needs to have at least three of ↑ nucleus-cytoplasm ratio, ↑ cellularity, prominent nucleus, unorganized growth, focal necrosis
- WHO grade III
 - Malignant; ↑ mitotic index with atypical cells, brain tissue infiltration, multifocal necrosis

TREATMENT

- Monitoring
 - Lesions small, asymptomatic

SURGERY

- Resection
 - Large symptomatic/asymptomatic tumors
- Stereotactic radiosurgery
 - Hard-to-reach/smaller than 3cm/1.18in lesions

OTHER INTERVENTIONS

- Radiotherapy
 - Primary management/adjuvant therapy

OLIGODENDROGLIOMA

osms.it/oligodendroglioma

PATHOLOGY & CAUSES

- A tumor derived from **oligodendrocytes**
- Supratentorial in frontal/temporal white matter (usual); spinal cord (occasional)
- Genetic alteration combination → oligodendroglioma grade II development → oligodendroglioma grade III progression
- Oligodendroglioma grade III can develop without oligodendroglioma grade II

TYPES

WHO classification

- Grade II
 - Low-grade, low mitotic index with atypical nuclei
- Grade III
 - High-grade (anaplastic), ↑ cellular density, ↑ mitotic index with atypical nuclei, microvascular proliferation
- Oligodendroglioma not-other-specified (NOS)
 - Tumors with appropriate histologic characteristics without 19p-1q chromosomes co-deletion or *IDH1/IDH2* gene mutation

CAUSES

- *IDH1/IDH2* gene mutation
- 19p-1q chromosomes co-deletion due to unbalanced translocation

RISK FACTORS

- Biologically-female > biologically-male individuals, aged 25–45, most commonly affected

SIGNS & SYMPTOMS

- May be asymptomatic; slow tumor growth
- Seizures
 - Focal/secondarily generalized
- Focal symptomatology
 - **Frontal lobe**: one-sided muscle weakness, impaired sensory perception, impaired memory
 - **Temporal lobe**: impaired language

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- T1 hypointense/T2 hyperintense mass

CT scan

- Hypodense, delineated tumor mass with calcification present

LAB RESULTS

- Genetic testing
 - *IDH* gene mutation, 19p-1q detection

OTHER DIAGNOSTICS

Histology

- Needed for diagnosis
 - Diffuse infiltrative tumors
 - Large nuclei with perinuclear halo—“fried egg” appearance
 - ↑ capillary branching—“chicken wire” appearance

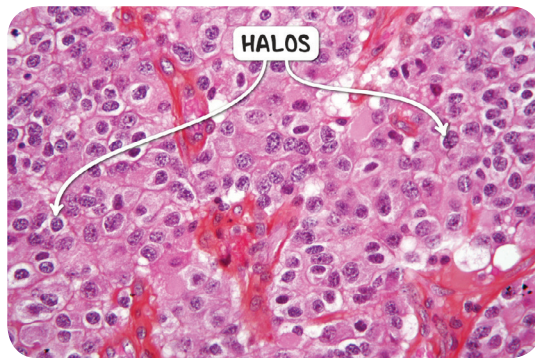


Figure 61.7 The histological appearance of an oligodendroglioma. The tumor is composed of monomorphic malignant glial cells with perinuclear halos and visible nucleoli.

TREATMENT

MEDICATIONS

- Chemotherapy

SURGERY

- Resection

OTHER INTERVENTIONS

- Radiation therapy